[0005] Modulation of microbial species in the GI tract through the use of antibiotics, antifungals, and more recently, fecal microbial transplantation ("FMT"), have been approaches clinically investigated for the treatment and/or prevention of certain diseases and disorders. For example, Dodd *et al.* (*Nature*, 2007, 551: 648-652) have proposed FMT as a therapeutic to modulate the levels of aromatic amino acid metabolites in the serum of gnotobiotic mice, which affect intestinal permeability and systemic immunity. In further examples, administration of bacterial compositions has also been proposed as a method for treating *Clostridium difficile* infection, ulcerative colitis, cholestatic disease, and hyperoxaluria (*see e.g.*, US 2018/0353554, WO 2019/036510, US RE39,585).

[0006] As a modality for treating various diseases and/or conditions, there is a need for microbial compositions comprising a plurality of microbial species having improved therapeutic efficacy and an ability to efficiently engraft in a host, grow, and metabolize pathogenic substrates to non-pathogenic metabolic products within the various biological niches of the GI tract and within the diverse GI environments of different individuals.

SUMMARY

[0007] Disclosed here is a microbial consortium for administration to an animal comprising a plurality of active microbes and an effective amount of a supportive community of microbes. In one aspect, the present disclosure provides a pharmaceutical composition comprising a microbial consortium comprising: a plurality of active microbes comprising *Oxalobacter formigenes*, an effective amount of a supportive community of microbes, and a pharmaceutically acceptable carrier or excipient, wherein the plurality of active microbes metabolizes oxalate to produce formate, and the supportive community of microbes comprises between 1 and 300 microbial strains, and catalyzes synthesis of methane from formate and H_2.

[0007a] In another aspect, the present disclosure provides a pharmaceutical composition comprising a microbial consortium comprising: a plurality of active microbes, an effective amount of a supportive community of microbes, and a pharmaceutically acceptable carrier or excipient, wherein the plurality of active microbes metabolizes a primary bile acid and the supportive community of microbes comprises between 1 and 300 microbial strains, wherein the plurality of active microbes comprises one or more microbial species selected from the group consisting of Bacteroides finegoldii, Bacteroides stercoris, Bacteroides fragilis, Bacteroides ovatus, Bacteroides vulgatus, Bacteroides dorei, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides eggerthii, Bacteroides rodentium, Bacteroides intestinalis, Bacteroides salyersiae, Bacteroides xylanisolvens, and Parabacteroides distasoni, optionally wherein the bile acid is lithocholic acid (LCA) or deoxycholic acid (DCA).

[0007b] In another aspect, the present disclosure provides a use of the pharmaceutical composition as described herein in the manufacture of a medicament for treating a subject diagnosed with or at risk for a metabolic disease or condition selected from the group consisting of primary hyperoxaluria, secondary hyperoxaluria, primary sclerosing cholangitis, primary biliary cholangitis, progressive familial intrahepatic cholestasis, nonalcoholic steatohepatitis, and multiple sclerosis.

[0007c] In some examples, the plurality of active microbes metabolize a first metabolic substrate to produce one or more than one metabolite, wherein the first metabolic substrate causes or contributes to disease in an animal.

[0008] In some examples, the supportive community of microbes comprises between 1 and 300 microbial strains and meets one, two, three, or four of the following conditions:

1) the supportive community of microbes metabolizes one or more than one metabolite produced by the plurality of active microbes, wherein the one or more than one metabolite inhibits metabolism of the first metabolic substrate by one or more of the plurality of active microbes,

2) the supportive community of microbes increases the flux of a precursor of the first metabolic substrate into a biochemical pathway that converts said precursor into a metabolite that is not the first metabolic substrate,

3) the supportive community of microbes enhances one or more than one characteristic of the plurality of active microbes when administered to an animal selected from the group consisting of: a) gastrointestinal engraftment, b) biomass, c)

CLAIMS

1. A pharmaceutical composition comprising a microbial consortium comprising:
   a plurality of active microbes comprising *Oxalobacter formigenes*, an effective amount of a supportive community of microbes, and a pharmaceutically acceptable carrier or excipient, wherein
   the plurality of active microbes metabolizes oxalate to produce formate, and
   the supportive community of microbes comprises between 1 and 300 microbial strains and catalyzes synthesis of methane from formate and H_2.
2. The pharmaceutical composition of claim 1, wherein the supportive community of microbes comprises
   a. at least three phyla selected from the group consisting of Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, Verrucomicrobia, and Euryarchaeota;
   b. at least four phyla selected from the group consisting of Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, Verrucomicrobia, and Euryarchaeota;
   c. at least five phyla selected from the group consisting of Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, Verrucomicrobia, and Euryarchaeota;
   d. at least six phyla selected from the group consisting of Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, Verrucomicrobia, and Euryarchaeota,
   e. the subclade Bacteroidales;
   f. the subclade Clostridiales;
   g. the subclade Erysipelotrichales;
   h. the subclade Negativicutes;
   i. the subclade Coriobacteriia;
   j. the subclade Bifidobacteriales; and/or
   k. the subclade Methanobacteriales.

3. The pharmaceutical composition of claim 1 or 2, wherein the supportive community of microbes comprises
   a. a Bacteroidetes and a Euryarchaeota;
   b. a *Bacteroides* and *Methanobrevibacter*; or

c. a *Bacteroides thetaiotaomicron* and/or *Bacteroides vulgatus*, and *Methanobrevibacter smithii*.

4. The pharmaceutical composition of claim 3, wherein the supportive community of microbes comprises between 20 and 200 microbial strains.

5. The pharmaceutical composition of claim 4, wherein the supportive community comprises at least 4 phyla selected from the group consisting of Bacteroidetes, Firmicutes, Actinobacteria, and Proteobacteria.

6. The pharmaceutical composition of claim 5, wherein the supportive community comprises
   a. a *Ruminococcus*, *Clostridium*, *Bacteroides*, *Neglecta*, *Bifidobacterium*, *Egerthella*, *Clostridiaceae*, *Parabacteroides*, *Bilophila*, *Dorea*, *Collinsella*, and *Faecalibacterium*;
   b. *a Ruminococcus bromii, Clostridium citroniae, Bacteroides salyersiae, Neglecta timonensis, Bifidobacterium longum, Bifidobacterium pseudocatenulatum, Bacteroides thetaiotaomicron, Eggerthella lenta, Clostridiaceae sp., Bifidobacterium dentium, Parabacteroides merdae, Bilophila wadsworthia, Bacteroides caccae, Dorea longicatena, Collinsella aerofaciens, Clostridium scindens, Faecalibacterium prausnitzii, Clostridium symbiosum*, and *Bacteroides vulgatus;*
   c. an *Acidaminococcus*, an *Akkermansia*, an *Alistipes*, an *Anaerofustis*, an *Anaerostipes*, an *Anaerotruncus*, a *Bacteroides*, a *Barnesiella*, a *Bifidobacterium*, a *Bilophila*, a *Blautia*, a *Butyricimonas*, a *Catabacter hongkongensis*, a *Clostridiaceae*, a *Clostridiales*, a *Clostridium*, a *Collinsella*, a *Coprococcus*, a *Dialister*, a *Dielma, a Dorea*, an *Eggerthella*, an *Eisenbergiella*, a *Eubacterium*, a *Faecalibacterium*, a *Fusicatenibacter saccharivorans*, a G*ordonibacter pamelaeae*, a *Holdemanella*, a *Hungatella*, a *Lachnoclostridium, Lachnospiraceae*, a *Lactobacillus*, a *Longicatena*, a *Megasphaera*, a *Methanobrevibacter*, a *Monoglobus*, a *Neglecta*, a *Parabacteroides*, a *Paraprevotella*, a *Parasutterella*, a *Phascolarctobacterium*, a *Porphyromonas*, a *Roseburia hominis*, a *Ruminococcaceae*, a *Ruminococcus*, a *Ruthenibacterium*, a *Senegalimassilia*, a *Sutterella*, and a *Turicibacter*; or

d. *Acidaminococcus intestine, Akkermansia muciniphila, Alistipes onderdonkii, Alistipes putredinis, Alistipes senegalensis, Alistipes shahii, Alistipes sp., Alistipes timonensis, Anaerofustis stercorihominis, Anaerostipes hadrus, Anaerotruncus massiliensis, Bacteroides caccae, Bacteroides coprocola, Bacteroides faecis, Bacteroides finegoldii, Bacteroides fragilis, Bacteroides kribbi, Bacteroides massiliensis, Bacteroides nordii, Bacteroides ovatus, Bacteroides salyersiae, Bacteroides stercorirosoris, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Bacteroides xylanisolvens, Barnesiella intestinihominis, Bifidobacterium adolescentis, Bifidobacterium bifidum, Bifidobacterium catenulatum, Bifidobacterium dentium, Bifidobacterium longum, Bifidobacterium pseudocatenulatum, Bilophila wadsworthia, Blautia faecis, Blautia hydrogenotrophica, Blautia massiliensis, Blautia obeum, Blautia wexlerae, Butyricimonas faecihominis, Catabacter hongkongensis, Clostridiaceae sp., Clostridiales sp., Clostridium aldenense, Clostridium bolteae, Clostridium citroniae, Clostridium clostridioforme, Clostridium fessum, Clostridium scindens, Collinsella aerofaciens, Coprococcus comes, Coprococcus eutactus, Dialister invisus, Dialister succinatiphilus, Dielma fastidiosa, Dorea formicigenerans, Dorea longicatena, Eggerthella lenta, Eisenbergiella tayi, Eubacterium eligens, Eubacterium hallii, Eubacterium rectale, Eubacterium siraeum, Eubacterium ventriosum, Eubacterium xylanophilum, Faecalibacterium prausnitzii, Fusicatenibacter saccharivorans, Gordonibacter pamelaeae, Holdemanella biformis, Hungatella effluvia, Lachnoclostridium pacaense, Lachnospiraceae sp., Lactobacillus rogosae, Longicatena caecimuris, Megasphaera massiliensis, Methanobrevibacter smithii, Monoglobus pectinilyticus, Neglecta timonensis, Parabacteroides distasonis, Parabacteroides merdae, Paraprevotella clara, Parasutterella excrementihominis, Phascolarctobacterium faecium, Porphyromonas asaccharolytica, Roseburia hominis, Ruminococcaceae sp., Ruminococcus bromii, Ruminococcus faecis, Ruthenibacterium lactatiformans, Senegalimassilia anaerobia, Sutterella massiliensis, Sutterella wadsworthensis,* and *Turicibacter sanguinis.*

7. The pharmaceutical composition of claim 6, wherein the supportive community consists of *Acidaminococcus intestine, Akkermansia muciniphila, Alistipes onderdonkii, Alistipes putredinis, Alistipes senegalensis, Alistipes shahii, Alistipes sp., Alistipes timonensis, Anaerofustis stercorihominis, Anaerostipes hadrus, Anaerotruncus massiliensis, Bacteroides caccae, Bacteroides coprocola, Bacteroides faecis, Bacteroides finegoldii, Bacteroides fragilis, Bacteroides kribbi, Bacteroides massiliensis, Bacteroides nordii, Bacteroides ovatus, Bacteroides salyersiae, Bacteroides stercorirosoris, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Bacteroides xylanisolvens, Barnesiella intestinihominis, Bifidobacterium adolescentis, Bifidobacterium bifidum, Bifidobacterium catenulatum, Bifidobacterium dentium, Bifidobacterium longum, Bifidobacterium pseudocatenulatum, Bilophila wadsworthia, Blautia faecis, Blautia hydrogenotrophica, Blautia massiliensis, Blautia obeum, Blautia wexlerae, Butyricimonas faecihominis, Catabacter hongkongensis, Clostridiaceae sp., Clostridiales sp., Clostridium aldenense, Clostridium bolteae, Clostridium citroniae, Clostridium clostridioforme, Clostridium fessum, Clostridium scindens, Collinsella aerofaciens, Coprococcus comes, Coprococcus eutactus, Dialister invisus, Dialister succinatiphilus, Dielma fastidiosa, Dorea formicigenerans, Dorea longicatena, Eggerthella lenta, Eisenbergiella tayi, Eubacterium eligens, Eubacterium hallii, Eubacterium rectale, Eubacterium siraeum, Eubacterium ventriosum, Eubacterium xylanophilum, Faecalibacterium prausnitzii, Fusicatenibacter saccharivorans, Gordonibacter pamelaeae, Holdemanella biformis, Hungatella effluvia, Lachnoclostridium pacaense, Lachnospiraceae sp., Lactobacillus rogosae, Longicatena caecimuris, Megasphaera massiliensis, Methanobrevibacter smithii, Monoglobus pectinilyticus, Neglecta timonensis, Parabacteroides distasonis, Parabacteroides merdae, Paraprevotella clara, Parasutterella excrementihominis, Phascolarctobacterium faecium, Porphyromonas asaccharolytica, Roseburia hominis, Ruminococcaceae sp., Ruminococcus bromii, Ruminococcus faecis, Ruthenibacterium lactatiformans, Senegalimassilia anaerobia, Sutterella massiliensis, Sutterella wadsworthensis,* and *Turicibacter sanguinis*.

8. The pharmaceutical composition of claim 5, wherein the supportive community comprises an *Akkermansia*, an *Alistipes*, an *Anaerostipes*, a *Bacteroides*, a *Bifidobacterium*, a *Bilophila*, a *Blautia*, a *Clostridium*, a *Collinsella aerofaciens*, a *Coprococcus*, *Dialister*, a *Dorea*, an

Eggerthella, an *Eisenbergiella*, a *Eubacterium*, a *Faecalibacterium*, a *Fusicatenibacter*, a *Gordonibacter*, a *Holdemanella*, a *Hungatella*, a *Lachnoclostridium*, a *Lachnospiraceae*, a *Lactobacillus*, a *Monoglobus*, a *Neglecta*, a *Parabacteroides*, a *Paraprevotella*, a *Parasutterella*, a *Phascolarctobacterium*, a *Porphyromonas*, a *Roseburia*, a *Ruminococcaceae*, a *Ruminococcus*, a *Ruthenibacterium*, and a *Sutterella*.

9. The pharmaceutical composition of claim 8, wherein the supportive community comprises *Akkermansia muciniphila*, *Alistipes onderdonkii*, *Alistipes putredinis*, *Alistipes shahii*, *Alistipes timonensis*, *Anaerostipes hadrus*, *Bacteroides caccae*, *Bacteroides fragilis*, *Bacteroides kribbi*, *Bacteroides koreensis*, *Bacteroides massiliensis*, *Bacteroides nordii*, *Bacteroides salyersiae*, *Bacteroides stercorirosoris*, *Bacteroides stercoris*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Bacteroides xylanisolvens*, *Bifidobacterium adolescentis*, *Bifidobacterium catenulatum*, *Bifidobacterium dentium*, *Bifidobacterium longum*, *Bifidobacterium pseudocatenulatum*, *Bilophila wadsworthia*, *Bilophila wadsworthia*, *Blautia faecis*, *Blautia obeum*, *Blautia wexlerae*, *Clostridium aldenense*, *Clostridium bolteae*, *Clostridium citroniae*, *Clostridium clostridioforme*, *Clostridium fessum*, *Clostridium scindens*, *Collinsella aerofaciens*, *Coprococcus comes*, *Coprococcus eutactus*, *Dialister invisus*, *Dialister succinatiphilus*, *Dorea formicigenerans*, *Dorea longicatena*, *Eggerthella lenta*, *Eisenbergiella tayi*, *Eubacterium eligens*, *Eubacterium rectale*, *Faecalibacterium prausnitzii*, *Fusicatenibacter saccharivorans*, *Gordonibacter pamelaeae*, *Holdemanella biformis*, *Hungatella effluvia*, *Lachnoclostridium pacaense*, *Lachnospiraceae sp.*, *Lactobacillus rogosae*, *Monoglobus pectinilyticus*, *Neglecta timonensis*, *Parabacteroides distasonis*, *Parabacteroides merdae*, *Paraprevotella clara*, *Parasutterella excrementihominis*, *Phascolarctobacterium faecium*, *Porphyromonas asaccharolytica*, *Roseburia hominis*, *Ruminococcaceae sp.*, *Ruminococcus bromii*, *Ruminococcus faecis*, *Ruthenibacterium lactatiformans*, *Sutterella massiliensis*, and *Sutterella wadsworthensis*.

10. The pharmaceutical composition of claim 8, wherein the supportive community consists of *Akkermansia muciniphila*, *Alistipes onderdonkii*, *Alistipes putredinis*, *Alistipes shahii*, *Alistipes timonensis*, *Anaerostipes hadrus*, *Bacteroides caccae*, *Bacteroides fragilis*,

Bacteroides kribbi, Bacteroides koreensis, Bacteroides massiliensis, Bacteroides nordii, Bacteroides salyersiae, Bacteroides stercorirosoris, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Bacteroides xylanisolvens, Bifidobacterium adolescentis, Bifidobacterium catenulatum, Bifidobacterium dentium, Bifidobacterium longum, Bifidobacterium pseudocatenulatum, Bilophila wadsworthia, Bilophila wadsworthia, Blautia faecis, Blautia obeum, Blautia wexlerae, Clostridium aldenense, Clostridium bolteae, Clostridium citroniae, Clostridium clostridioforme, Clostridium fessum, Clostridium scindens, Collinsella aerofaciens, Coprococcus comes, Coprococcus eutactus, Dialister invisus, Dialister succinatiphilus, Dorea formicigenerans, Dorea longicatena, Eggerthella lenta, Eisenbergiella tayi, Eubacterium eligens, Eubacterium rectale, Faecalibacterium prausnitzii, Fusicatenibacter saccharivorans, Gordonibacter pamelaeae, Holdemanella biformis, Hungatella effluvia, Lachnoclostridium pacaense, Lachnospiraceae sp., Lactobacillus rogosae, Monoglobus pectinilyticus, Neglecta timonensis, Parabacteroides distasonis, Parabacteroides merdae, Paraprevotella clara, Parasutterella excrementihominis, Phascolarctobacterium faecium, Porphyromonas asaccharolytica, Roseburia hominis, Ruminococcaceae sp., Ruminococcus bromii, Ruminococcus faecis, Ruthenibacterium lactatiformans, Sutterella massiliensis, and *Sutterella wadsworthensis.*

11. The pharmaceutical composition of any one of claims 1-10, wherein the microbial consortium or the supportive community of microbes comprises
    a. 20 to 200 microbial strains.
    b. 70 to 80 microbial strains;
    c. 80 to 90 microbial strains;
    d. 100 to 110 microbial strains; or
    e. 150 to 160 microbial strains.

12. The pharmaceutical composition according to any one of claims 1 to 11, wherein the microbial consortium, upon administration to an animal on a high oxalate diet, reduces oxalate concentration in a sample selected from the group consisting of blood, serum, stool,

or urine, as compared to a sample collected from a corresponding control animal on a high oxalate diet that has not been administered with the microbial consortium.

13. The pharmaceutical composition according to any one of claims 1 to 12, wherein the plurality of active microbes comprises 3 *Oxalobacter formigenes* strains.

14. The pharmaceutical composition according to any one of claim 1 to 13, wherein the microbial consortium or the supportive community of microbes comprises
    a. 20 to 200 microbial strains;
    b. 70 to 80 microbial strains;
    c. 80 to 90 microbial strains;
    d. 100 to 110 microbial strains; or
    e. 150 to 160 microbial strains.

15. A pharmaceutical composition comprising a microbial consortium comprising: a plurality of active microbes, an effective amount of a supportive community of microbes, and a pharmaceutically acceptable carrier or excipient, wherein the plurality of active microbes metabolizes a primary bile acid and the supportive community of microbes comprises between 1 and 300 microbial strains, wherein the plurality of active microbes comprises one or more microbial species selected from the group consisting of Bacteroides finegoldii, Bacteroides stercoris, Bacteroides fragilis, Bacteroides ovatus, Bacteroides vulgatus, Bacteroides dorei, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides eggerthii, Bacteroides rodentium, Bacteroides intestinalis, Bacteroides salyersiae, Bacteroides xylanisolvens, and Parabacteroides distasoni, optionally
    wherein the bile acid is lithocholic acid (LCA) or deoxycholic acid (DCA).

16. The pharmaceutical composition of claim 15, wherein the one or more than one metabolite is selected from the group consisting of iso-lithocholic acid (iso-LCA), or iso-deoxycholic acid (iso-DCA).

17. The pharmaceutical composition according to any one of claims 15 to 16, wherein the supportive community of microbes enhances the conversion of
    a. one or more conjugated bile acids selected from the group consisting of taurochenodeoxycholic acid (TCDCA), glycochenodeoxycholic acid (GCDCA), taurocholic acid (TCA), and glycocholic acid (GCA), to cholic acid (CA) or chenodeoxycholic acid (CDCA);
    b. CA to 7-beta-cholic acid (7betaCA); and/or
    c. CDCA to ursodeoxycholic acid (UDCA).

18. The pharmaceutical composition according to any one of claims 15 to 17, wherein the plurality of active microbes comprises one or more microbial phyla selected from Firmicutes and Actinobacteria.

19. The pharmaceutical composition of claim 18, wherein the plurality of active microbes comprises one or more microbial strain selected from *Eggerthella lenta* and *Clostridium scindens.*

20. The pharmaceutical composition according to any one of claims 15 to 19, wherein the microbial consortium or the supportive community of microbes comprises
    a. 20 to 200 microbial strains.
    b. 70 to 80 microbial strains;
    c. 80 to 90 microbial strains;
    d. 100 to 110 microbial strains; or
    e. 150 to 160 microbial strains.

21. The pharmaceutical composition according to any one of claims 1 to 20, wherein the microbial consortium is to be administered as a pre-determined dose in a range from 1 X 10^6 total CFU to 1 X 10^{13} total CFU.

22. Use of the pharmaceutical composition according to any one of claims 1 to 21 in the manufacture of a medicament for treating a subject diagnosed with or at risk for a metabolic

disease or condition selected from the group consisting of primary hyperoxaluria, secondary hyperoxaluria, primary sclerosing cholangitis, primary biliary cholangitis, progressive familial intrahepatic cholestasis, nonalcoholic steatohepatitis, and multiple sclerosis.

23. The use of claim 22, wherein administration of the pharmaceutical composition reduces levels of the first metabolic substrate in the subject by
    a. at least 20% as compared to an untreated control subject or as compared to pre-administration levels of the first metabolic substrate in the subject;
    b. at least 40% as compared to an untreated control subject or as compared to pre-administration levels of the first metabolic substrate in the subject;
    c. at least 60% as compared to an untreated control subject or as compared to pre-administration levels of the first metabolic substrate in the subject; or
    d. at least 80% as compared to an untreated control subject or as compared to pre-administration levels of the first metabolic substrate in the subject.

24. The use according to claim 23, wherein the first metabolic substrate is oxalate or DCA or LCA.

25. The use according to claim 23, wherein the level of first metabolic substrate is determined from a blood, serum, stool, or urine sample.